Posttraumatic Stress Disorder: A mind-body response to life-threatening events

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Imagine: you are peacefully asleep in your bed when suddenly you are awakened by a voice that says, "I have a knife, so don't make any noise." You wonder if you are having a nightmare but as you awaken more fully, you feel the point of the knife at your throat. You begin to hyperventilate as you experience complete terror. You feel frozen — both mentally and physically.

This is an example of an event that nearly everyone would find traumatic – a sudden, unexpected, life-threatening assault. When researchers began studying traumatic stress, and in particular posttraumatic stress disorder (PTSD), they assumed that the psychological and biological processes would be related in essential ways to the normal response to stress. However, while normal stress responses are acute reactions that quickly return to homeostasis, the mind and body responses in PTSD reflect chronic and often increasing changes over time. Even when stress is chronic, the results differ from those of traumatic stress. The effects of chronic stress develop slowly over time, whereas the effects of traumatic stress are sudden and dramatic and are marked by fear, helplessness and horror.

PTSD was first labeled as such in 1980, following the Vietnam War. Prior to that time, there had been only periodic interest in traumatic stress, usually in times of armed conflict, and it was known under various names, such as traumatic neurosis, shell shock or concentration camp syndrome. PTSD, however, has gained increasing attention in the last quarter of a century with the rise in military missions abroad, natural disasters, technical and traffic accidents, and domestic violence – the latter, though, still given short shrift in most PTSD studies.

What is PTSD?

According to the contemporary diagnostic systems for psychiatric disorders, six criteria must be met before a diagnosis of PTSD can be made. The first, criterion A, is the stressor criterion. It states that a person must have experienced, witnessed or been confronted with an event that involved actual or threatened death or serious injury, or a threat to the physical integrity of the person or others.

The second criterion, B, reflects reexperiencing symptoms. The most dramatic form of reexperiencing is the flashback. Here the patient feels and acts as if the trauma is recurring. Reexperiencing also includes distressing memories or dreams (nightmares) when faced with stimuli linked to the traumatic event. There may be physiological or psychological stress reactions – including full-blown panic attacks – associated with this reexperiencing.

Avoidance and numbing symptoms comprise the third criterion, C. Patients with PTSD may attempt to avoid trauma-related thoughts or activities. They may show a notably diminished capacity to experience pleasure, difficulty in remembering aspects of the trauma, blunted affect and feelings of detachment or estrangement from others.

Symptoms of hyperarousal and hypervigilance are represented in criterion D. They include pervasive arousal that is reflected by difficulties in concentration, irritability and problems in falling and staying asleep. Also included are exaggerated startle responses to a variety of cues.

The fifth criterion, E, for the diagnosis is that the B, C and D symptoms persist for at least 1 month. The sixth criterion, F, is that this combination of symptoms causes significant distress for the person or impairment in his/her social or professional functioning. Criterion F specifies that a diagnosis of psychopathology should not be made if the symptoms are mild or do not really interfere with a person's life.

When the PTSD diagnosis was introduced in 1980, it was believed that traumatic events sufficient to induce this condition would be rare. However, subsequent epidemiologic surveys have documented a high prevalence of such events, with one- to two-thirds of the population receiving exposure to trauma over the course of a lifetime. In first world countries, the most common traumatic events are witnessing a severe injury or death and/or involvement in a fire, other natural disaster or life-threatening accident. Rape, sexual and physical abuse, and parental neglect are more common among women than men. Men are more likely to experience physical attack or military-related trauma.

In countries of the northern hemisphere, the lifetime prevalence of PTSD (i.e. the chance of suffering PTSD at least once during one's life) is approximately 5%. The rate is obviously significantly higher in war-stricken countries or countries with especially high rates of crime or natural catastrophies.

PTSD is not the only psychiatric disorder that may develop after a traumatic experience. Depression and anxiety disorders may result independently of PTSD or may be comorbid with it. Clinicians often observe that other disorders develop as maladaptive coping attempts and then become full-blown problems in and of themselves. For example, if someone has severe PTSD symptoms including nightmares, sleep disruption, flashbacks, hypervigilance and other physiological arousal symptoms, that person may attempt to reduce his/her suffering by consuming alcohol or illegal drugs. Not uncommonly, somatic diseases may be comorbid with PTSD. Studies in the elderly have reported direct links between trauma and a broad spectrum of medical conditions (diabetes mellitus, heart disease, obesity and osteoarthritis) in 20- or 30-year follow-ups of men initially exposed to traumatic stress.

This brings us to the point where we can begin to consider the numerous ways in which the mind and body interact in PTSD. This relationship functions in all stages of the development and manifestation of PTSD, from risk and resilience factors through to the core psychobiological changes associated with PTSD. The development of successful therapies for PTSD is also fundamentally dependent on understanding how the mind and body can synchronously and mutually respond to and cope with real and perceived threats to their integrity.

Early life trauma as a risk factor

Because people show varying responses to similar traumatic events, it is likely that the trauma itself is not solely responsible for causing the posttrauma symptoms. This realization has led to the search for factors that may increase the risk of developing PTSD after trauma. One such factor that has recently received considerable attention from researchers is the victim's psychological history or prior experience with trauma.

Until the last decade, the hypothesis that early life trauma is associated with an increased risk of adult PTSD or other psychiatric disorders was supported largely by anecdotal reports inspired by psychoanalytic concepts of early critical periods of development. The best research in the neurobiology of depression has commonly found indications of early life stress. How about the role of early life trauma in victims who develop PTSD?

Valid data to examine the correlation between early trauma and later PTSD (or depression) are, in fact, surprisingly sparse and are derived mainly from small samples or spontaneous reports of trauma from social service departments or hospital emergency rooms. Reported cases of early trauma constitute a relatively small fraction of all cases; however, although prevalence estimates of childhood abuse and other traumas such as early loss of parents are extremely approximate, they are indeed sufficient to account in part for the development of PTSD after trauma (or depression) among the general adult population.

A study in the USA by McCauley and colleagues [1] of nearly 2,000 women from all socioeconomic classes attending four community-based primary care internal medicine practices found a 22% prevalence of reported childhood or adolescent physical or sexual abuse or severe neglect. Compared with the remainder of the sample, those with childhood trauma reported significantly more physical symptoms, as well as significantly higher scores for depression, anxiety, somatization and interpersonal sensitivity, a fivefold higher prevalence of drug abuse and a twofold higher level of alcohol abuse. Unfortunately, PTSD diagnoses were not studied.

More recently, we investigated a representative sample of approximately 2,000 young women from Dresden (Germany) for the occurrence of traumatic events and the development of PTSD and depression [2]. Although the prevalence of childhood trauma of 11% was lower than in the US study, risks for PTSD and depressive disorder were 17% and 23%, respectively. Interestingly, the equal risk of later PTSD or depression is in line with other research findings on psychopathological vulnerability in humans.

By and large, these data support the general models of vulnerability to PTSD or depressive disorder which posit that genetic factors, temperament, and trauma early and later in life markedly increase the risk of these conditions. When superimposed on this background of risk, recently experienced traumatic events trigger these psychiatric disorders. This effect is partly mediated by the hormone corticotropin-releasing factor (CRF), which plays a key role in modulating the autonomic, immune and behavioral effects of all kinds of stress. Increases in CRF are associated with increased symptoms of PTSD and depression.

Is this general model consistent with animal research findings linking early trauma with hypothalamic-pituitary-adrenal (HPA) axis functioning? In a rat model of neglect, rat pups were removed from their mothers for 3 hours daily between the ages of 2–14 days and then returned to their mothers in the animal colony for a week before weaning; this naturalistic stressor is thought to be analogous to neglect in human childhood

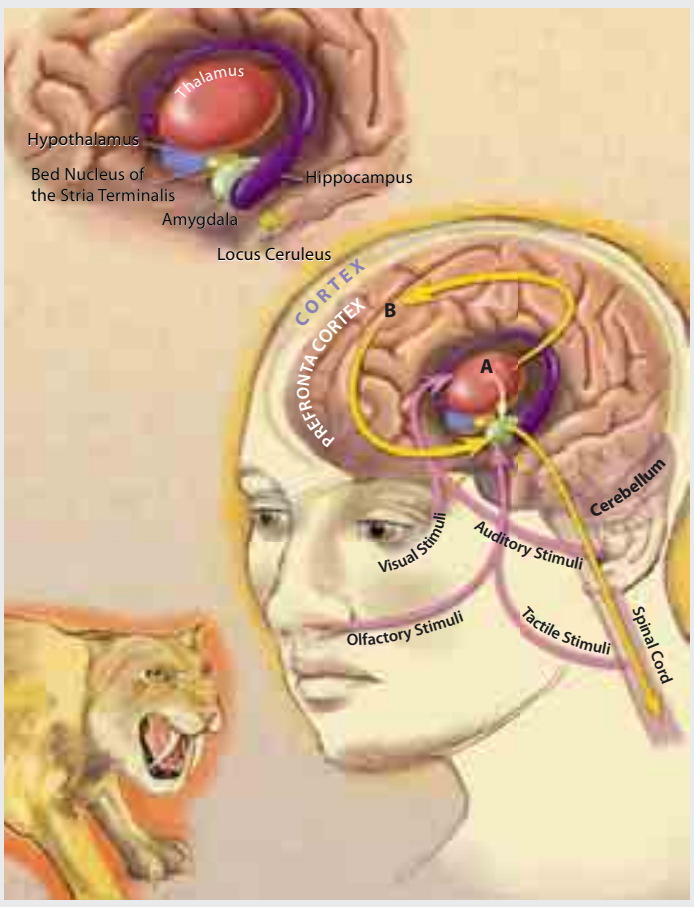

Fig. 1. Body's response to a threat or perceived threat (see box 1 for details). [Reprinted from ref. 8 with permission from Elsevier. After a diagram in the June 10, 2002 issue of *Time* Magazine.]

up to the age of 4–5 years [3]. Researchers found that rat pups subjected to this type of maternal deprivation at the age of 10 days had significant reductions in median eminence CRF concentrations after 24 hours, which can be interpreted as an increase in hypothalamic CRF release. However, the effect was seen only during a critical time window – maternal deprivation did not reduce CRF concentrations in older rat pups.

Can these animal findings on hormone responses to early life trauma be extended to the clinical arena dealing with patients? In a very interesting study, US researchers examined hormone levels (cortisol) of women in the emergency room, immediately after being raped [4]. Three months later, these woman were assessed for PTSD and were interviewed about their histories of trauma. The researchers found that the rape victims who also had a history of childhood sexual abuse were more likely to have PTSD after 3 months. They also found that the women with sexual abuse histories had lower cortisol levels soon after the rape than the women without such histories. This finding supports the idea that chronic trauma results in a distortion of the stress response and in a sensitization towards aggravated stress responses to newly experienced trauma.

Resilience factors

Aversive childhood experiences are certainly not the only known risk factor for PTSD. However, let us turn to the other side of the coin of PTSD development: resilience factors. Resilience toward aversive life events has been addressed since ancient times by authors as diverse as Confucius ("Our greatest glory is not in never falling, but in rising every time we fall") and Nietzsche ("That which does not kill us can only make us stronger").

A wealth of elements that comprise resilience have been proposed in the literature, including active problem-solving, responsibility, self-esteem, independence, well-being, initiative, humor, insight, creativity and many others. Measuring these concepts and understanding their respective roles presents a formidable challenge. One of the recently researched concepts is that of posttraumatic growth, referring to a positive psychological change arising from the struggle with a major life crisis. Only in recent years have positive changes following trauma and adversity been studied systematically. They have been reported empirically following highly stressful events such as severe physical illness, injury, rape and sexual assault, military combat, natural disasters and accidents.

Posttraumatic growth refers to psychological changes that include an identification of new possibilities, more meaningful interpersonal relationships, increased appreciation of life, changed priorities and an increased sense of personal strength and growth in the domain of spiritual and existential matters. It is not yet clear whether posttraumatic growth constitutes a more uniform resilience factor to subsequent PTSD or if it is a more complex phenomenon comprising realistic as well as illusory components [5]. However, it is interesting to study where it may work in the brain, i.e. which brain structures constitute this resilience factor.

Popular brain models suggest that positive emotionality and personal attitudes (e.g. goal-directed approach tendencies: challenging oneself and striving to achieve in the face of adversity) are constituted by left frontal brain activation. In contrast, dominance of right frontal brain activation is related to more negative emotionality and depression. In a study of 82 survivors of traffic accidents with PTSD, our group found that people who had high levels of posttraumatic growth (= positive psychological change marked by an active change of attitudes, goals and personal relations) also had higher levels of left-hemispheric frontal activation, while people who had lower levels of posttraumatic growth had lower activation in that area [6].

Again, a variety of other resilience factors have been formulated and investigated, including those that are constituted by interpersonal or community factors, e.g. having somebody to talk to or being socially supported by others after a trauma. More about such social resilience factors can be found in a recent book by Resick [7].

Neural circuits, memory and body reactions

So far, I have not discussed exactly how a trauma affects the mind and body. How do mind and body react to a sudden, overwhelming threat? The main components of the central nervous system that respond to threats are the thalamus (the gateway for sensory inputs), the hippocampus (which is involved in memory access) and the amygdala. The amygdala drives the initial response to a traumatic event, instigating what is classically known as the "fight or flight response." The clinical course is subsequently modified by memories managed in neural circuits between the hippocampus and the frontal brain (cortex).

Together, these brain structures coordinate how we experience threat and learn to avoid pain. As mentioned above, the amygdala is the primary responding structure. It has a twofold function. It recognizes danger signals rapidly through primitive visual pathways that bypass the cortex, evaluating objects in the environment before interacting with them. It can very quickly activate nearly every bodily system to engage the threat – or flee it. Signals from the amygdala, though, also enhance the processing of fear-inducing information by higher cortical structures, and the amygdala stimulates the hippocampus to help the brain learn and form danger-specific memories. The magnitude and experience of the threat and the subsequent reexperiencing, avoidance/numbing and hyperarousal/hypervigilance are important determinants in the clinical development of PTSD. Figure 1 and box 1 outline how the body responds to a threat.

Thus, initial responses to a traumatic stress are largely biological and driven by the amygdala, while the memories engendered by the hippocampus and the cognitive decisions made by the cortex will organize the mid- and long-term behavior of subjects exposed to traumatic stress. One way to understand PTSD is as a failure to recover from a universal set of immediate emotional and biological reactions to a traumatic stress: memory and adaptive responses malfunction, and with each exposure to a trauma-related stimulus, the subject is once more flooded by immediate-threat responses.

Neurobiological long-term outcomes may be the already described imbalances or distortions of stress hormones of the HPA axis (such as CRF and cortisol) or the persistent asymmetry of brain hemisphere activation in the frontal cortex. My group has been investigating in more depth the manifestations of brain asymmetry in PTSD [9]. Cognitive studies with PTSD sufferers have found that they reexperience symptoms of traumatic events very vividly, and usually visually. These trauma memories are quite different from the remembering of ordinary autobiographical memories, in which sensory elements are integrated into a personal narrative and which seems to be primarily dependent on the left hemisphere.

The study of traffic accident victims has supported these findings: PTSD patients displayed a pattern of increased right-sided activation during exposure to a trauma-related picture when compared with two other groups, traffic accidents survivors without PTSD and healthy, nontraumatized controls. The opposite pattern of relative left hemisphere activation during exposure to the trauma-related picture was observed in traffic accident survivors without PTSD. This latter finding might reflect more adaptive tendencies to process the threat experience by posttraumatic growth (as discussed above).

As mentioned earlier, neurobiological changes involve not only the brain but peripheral body regulation as well. An elevated heart rate has been a prominent marker for PTSD-related hyperarousal in the body. In early research on heart rate at rest (so-called baseline arousal), PTSD patients were found to have a higher resting heart rate than controls – by up to 10 beats per minute – while more recent studies have shown that the heart rate of PTSD patients is particularly elevated when they are being reminded of or are reexperiencing the trauma. Since a chronic heart rate elevation of this magnitude may cause medical complications in later

Box 1. Subcortical and cortical responses to threat

Immediate (subcortical) response to threat (A)

- Upon seeing or hearing a threat, visual and auditory stimuli arrive at the thalamus.
- This information immediately passes from the thalamus to the fear center in the amygdala. Olfactory and tactile stimuli are sent *directly* to the amygdala, bypassing the thalamus; they evoke stronger memories and feelings than do sights and sounds.
- The amygdala alerts other brain structures, including the hypothalamus and locus ceruleus. Somatic responses include sweaty palms, tachycardia, increased blood pressure and a surge in norepinephrine.
- The threatened individual is then prepared for a "fight or flight response."

Cognitive processing of threat (B)

- After fear activation, the thalamus sends information to the cortex for cognitive processing.
- The neocortex analyzes the data from the sensory organs and decides whether or not to continue the fear response.
- If the decision is to maintain the fear response, the amygdala remains on alert and the hippocampus is inhibited in the laying down of event-related memories. The hippocampus is the memory-organizing center of the brain and an important regulator of the stress response.

life, successful treatment of PTSD is needed not only for healing the wounds of the psyche but also such "wounds" of the body.

Treatment works

Two highly positive statements can be made with respect to the treatment of those suffering from trauma. First, we have recourse to several psychotherapeutic techniques that are highly effective for the majority of patients. Second, successful therapies are indeed able to correct the neurobiological distortions consequent to trauma that I have described above.

What is the evidence for the first statement? Although most therapists working with traumatized individuals use psychodynamic or supportive counseling approaches – for which there are no efficacy data – most studies of PTSD treatment outcomes have explored cognitive-behavioral therapy (CBT). CBT for PTSD includes two general subtypes of therapeutic technique. In exposure techniques such as systematic desensitization and flooding, patients confront their fears, object, situation, memories and images without being as overwhelmed as they had anticipated. These experiences of exposure thus serve to disconfirm and correct inner beliefs like "my memories will certainly drive me crazy." Cognitive techniques identify and challenge erroneous cognitions (e.g. "the world is unjust or malevolent," "bad things always happen to me"), aiming to replace them with more realistic cognitions. These procedures can be accompanied by an anxiety management component, which includes a variety of techniques such as relaxation, controlled breathing and self-distraction (thought stopping); patients carry out exercises designed to improve their anxiety management skills.

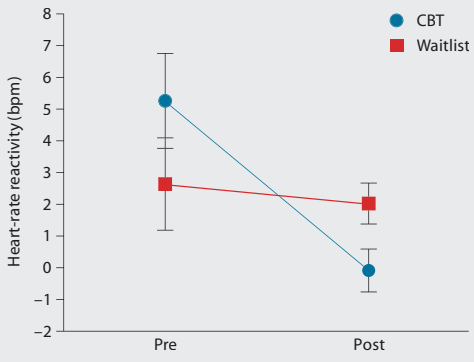

Fig. 2. Mean heart rate reactivity scores for a trauma-related picture in the CBT treatment group and a waiting list control group with no therapy, pre- and posttreatment [with permission from ref. 10]

In detail, particular CBT components for PTSD have been developed from a biopsychological understanding of this disorder. In PTSD, a wide range of psychological processes are disrupted, including attention, beliefs, cognitive-affective responses, memory, styles of coping and social-support systems, all of which need to be appropriately and adequately addressed during the course of treatment.

Box 2.
Eye movement desensitization and reprocessing (EMDR) is an effective combination of body-focused and cognitive-behavioral therapy developed by the psychologist Francine Shapiro in the early 1990s to help alleviate the distress associated with trauma. During EMDR, the client is asked to concentrate on the traumatic experience with its associated negative beliefs and sensations while simultaneously moving his or her eyes back and forth focusing on an external rhythmic stimulus such as hand movements by the therapist or alternating right-left sounds. The patient is then directed to concentrate on a positive thought (something that feels positive and safe), which is reinforced by the EMDR and replaces the negative one. How this actually works is unknown, and there exists some controversy about the necessity for all components of the therapy, especially the eye movements. Nevertheless, EMDR has been used successfully to desensitize anxiety in PTSD patients.

Strict evaluations of these psychotherapies by high-quality methodologies have shown a benefit of psychotherapy for most patients with PTSD. Comprehensive surveys of the available data (so-called metaanalyses) have amalgamated the results from numerous psychotherapy studies conducted between 1980 and 2005 and found that about two-thirds of patients with PTSD completing treatment with various forms of CBT or a new treatment developed specifically for PTSD – eye movement desensitization and reprocessing (EMDR; see box 2) – improve or recover fully.

Treatment studies with CBT or EMDR psychotherapies have also been able to show repair or reconstruction of distorted neurobiological processes in PTSD. When our own clinic treated traffic accident victims with PTSD, we assessed several biological processes before and after treatment. One focus was right-hemispheric activation during exposure to trauma-related pictures. The majority of patients who significantly improved during psychotherapy showed the same brain activity pattern as healthy control persons, namely relative left hemisphere activation during exposure, reflecting a turn to more adaptive tendencies to deal with the traumatic memories. Other research focused on heart rate changes in PTSD. Figure 2 shows a reduction of 5.5 heart beats per minute in those who received CBT. This is an important prophylactic diminution in a chronic cardiovascular handicap that can be triggered by the recall of traumatic experiences.

What, though, about the 30% of patients of all available psychotherapy studies who showed little or no improvement? What strategies might help them? Results on the full range of body and mind changes after trauma imply that instead of going through a single psychotherapy pathway to recovery, different treatment modalities may be able to modulate the system in different ways. Drug treatment of various kinds might act primarily via a subcortical ("bottom-up") approach and psychotherapeutic approaches primarily via a cortical ("top-down") approach. Subtyping PTSD according to the brain's states might also be an effective method for selecting the best treatment modality for a given patient.

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Published by S. Karger AG, Basel
Edited by Dagmar Horn and Anne Blonstein(*ab*)
Design by Erich Gschwind

The Karger Gazette is also available online.

www.karger.com/gazette

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